

Attorney Docket No.: PTQ-0028
Inventors: Van Eyk et al.
Serial No.: 09/419,901
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This listing of the claims will replace all prior versions and listings of claims in the application:

Listing of the claims:

Claim 1 (currently amended): A method for assessing muscle damage in a subject, comprising:

obtaining a biological sample from a subject being assessed for muscle damage; and

evaluating for the presence ~~or absence~~ of one or more different myofilament protein modification products in the biological sample, at least one of said myofilament protein modification products being a chemical adduct of a myofilament protein selected from the group consisting of troponin I, troponin T, troponin C, α -actinin, actin, tropomyosin, desmin, myosin light chain 1, myosin light chain 2, and myosin light chain 3; and

wherein the presence of at least one myofilament protein modification product which is a chemical adduct of a myofilament protein selected from the group consisting of troponin I, troponin T, troponin C, α -actinin, actin, tropomyosin, desmin, myosin light chain 1, myosin light chain 2, and myosin light chain 3 in the biological sample is indicative of muscle damage in said subject; and

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wherein the chemical adduct of the myofilament protein is a post-translational modification of an intact myofilament protein, a post-translational modification of a degradation product of a myofilament protein or a post-translational modification of a protein-protein complex of myofilament proteins and said myofilament protein is selected from the group consisting of troponin I, troponin T, troponin C, α -actinin, actin, tropomyosin, desmin, myosin light chain 1, myosin light chain 2, and myosin light chain 3.

Claim 2 (currently amended): The method of claim 1, further comprising the step of assessing the amount of the one or more different myofilament protein modification products present in the biological sample as an indication of the extent of muscle damage in the subject, wherein at least one of said myofilament protein modification products is a chemical adduct of a myofilament protein selected from the group consisting of troponin I, troponin T, troponin C, α -actinin, actin, tropomyosin, desmin, myosin light chain 1, myosin light chain 2, and myosin light chain 3.

Claim 3 (currently amended): The method of claim 1, wherein the evaluating step comprises detecting the presence

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of at least two different myofilament protein modification products in the biological sample, wherein at least one of said myofilament protein modification products is a chemical adduct of a myofilament protein selected from the group consisting of troponin I, troponin T, troponin C, α -actinin, actin, tropomyosin, desmin, myosin light chain 1, myosin light chain 2, and myosin light chain 3.

Claim 4 (currently amended): The method of claim 3, further comprising the step of assessing the amounts of said at least two different myofilament protein modification products present in the biological sample, and comparing the amounts as an indication of the extent of muscle damage in the subject, wherein at least one of said myofilament protein modification products is a chemical adduct of a myofilament protein selected from the group consisting of troponin I, troponin T, troponin C, α -actinin, actin, tropomyosin, desmin, myosin light chain 1, myosin light chain 2, and myosin light chain 3.

Claim 5 (currently amended): The method of claim 3, wherein said at least two different myofilament protein modification products are from the same protein, wherein at

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least one of said myofilament protein modification products is a chemical adduct of a myofilament protein selected from the group consisting of troponin I, troponin T, troponin C, α-actinin, actin, tropomyosin, desmin, myosin light chain 1, myosin light chain 2, and myosin light chain 3.

Claim 6 (currently amended): The method of claim 3, wherein said at least two different myofilament protein modification products are from different proteins, wherein at least one of said myofilament protein modification products is a chemical adduct of a myofilament protein selected from the group consisting of troponin I, troponin T, troponin C, α-actinin, actin, tropomyosin, desmin, myosin light chain 1, myosin light chain 2, and myosin light chain 3.

Claim 7 (currently amended): The method of claim 6, further comprising the step of assessing the ratio of said at least two different myofilament protein modification products as an indication of the extent of muscle damage in the subject, wherein at least one of said myofilament protein modification products is a chemical adduct of a myofilament protein selected from the group consisting of

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troponin I, troponin T, troponin C, α -actinin, actin,
tropomyosin, desmin, myosin light chain 1, myosin light
chain 2, and myosin light chain 3.

Claims 8-14 (canceled)

Claim 15 (original): The method of claim 1, wherein the muscle is selected from the group consisting of cardiac muscle and skeletal muscle.

Claim 16 (original): The method of claim 15, wherein the muscle damage is due to at least one condition selected from the group consisting of hypoxia, hypoxemia, ischemia, and reperfusion.

Claim 17 (original): The method of claim 16, wherein the muscle damage is reversible.

Claim 18 (original): The method of claim 16, wherein the muscle damage is irreversible.

Claim 19: (canceled)

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Claim 20 (currently amended): The method of ~~claim 19~~
claim 1, wherein at least one of the myofilament protein
modification products is a protein-protein complex
comprising at least two polypeptides, at least one of said
polypeptides being a chemical adduct of an intact protein or
a fragment of a protein selected from the group consisting
of troponin I, troponin T, troponin C, α -actinin, actin,
tropomyosin, desmin, myosin light chain 1, myosin light
chain 2, and myosin light chain 3.

Claim 21 (previously presented): The method of claim 1,
wherein at least one of the myofilament protein modification
products is a chemical adduct of a degradation product of a
myofilament protein selected from the group consisting of
troponin I, troponin T, troponin C, α -actinin, actin,
tropomyosin, desmin, myosin light chain 1, myosin light
chain 2, and myosin light chain 3.

Claim 22 (currently amended): The method of ~~claim 19~~
claim 1, wherein the chemical adduct of a myofilament
protein is a myofilament protein modified by post-
translational modification.

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Claim 23 (original): The method of claim 22, wherein the post-translational modification is selected from the group consisting of phosphorylation, glycosylation, myristylation, phenylation, acetylation, nitrosylation, and sulphation.

Claim 24 (original): The method of claim 20, wherein the chemical adduct of a myofilament protein is a protein-protein complex modified by post-translational modification.

Claim 25 (previously presented): The method of claim 24, wherein the post-translational modification is selected from the group consisting of phosphorylation, glycosylation, myristylation, phenylation, acetylation, nitrosylation, and sulphation.

Claim 26 (original): The method of claim 21, wherein the chemical adduct of a myofilament protein is a degradation product of a myofilament protein modified by post-translational modification.

Claim 27 (previously presented): The method of claim 26, wherein the post-translational modification is selected from the group consisting of phosphorylation, glycosylation,

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myristylation, phenylation, acetylation, nitrosylation, and sulphation.

Claim 28 (previously presented): The method of claim 1, wherein the muscle is cardiac muscle and the myofilament protein modification product is phosphorylated troponin I.

Claims 29-30 (canceled)

Claim 31 (previously presented): The method of claim 1, wherein the myofilament protein is myosin light chain 1.

Claims 32-33 (canceled)

Claim 34 (original): The method of claim 1, wherein the biological sample is selected from the group consisting of cardiac muscle tissue, a component of cardiac muscle tissue, blood, blood serum, blood plasma, skeletal muscle tissue, a component of skeletal muscle tissue, and urine.

Claim 35 (currently amended): A method for assessing muscle damage in a subject, comprising:

obtaining at least two biological samples from a subject being assessed for muscle damage; and

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evaluating for the presence ~~or absence~~ of one or more myofilament protein modification products in the biological samples;

wherein said biological samples are not obtained simultaneously;

wherein at least one of the myofilament protein modification products is a chemical adduct of a myofilament protein selected from the group consisting of troponin I, troponin T, troponin C, α -actinin, actin, tropomyosin, desmin, myosin light chain 1, myosin light chain 2, and myosin light chain 3; and

wherein the presence of one or more chemical adducts of a myofilament protein selected from the group consisting of troponin I, troponin T, troponin C, α -actinin, actin, tropomyosin, desmin, myosin light chain 1, myosin light chain 2, and myosin light chain 3 in at least one of said biological samples is indicative of muscle damage in the subject; and

wherein the chemical adduct of the myofilament protein selected from the group consisting of troponin I, troponin T, troponin C, α -actinin, actin, tropomyosin, desmin, myosin light chain 1, myosin light chain 2, and myosin light chain 3 is a post-translational modification of an intact

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myofilament protein, a post-translational modification of a degradation product of a myofilament protein or a post-translational modification of a protein-protein complex of myofilament proteins.

Claim 36 (canceled)

Claim 37 (currently amended): The method of claim 35, further comprising assessing a change with time in the presence or amount of one or more chemical adducts of a myofilament protein selected from the group consisting of troponin I, troponin T, troponin C, α -actinin, actin, tropomyosin, desmin, myosin light chain 1, myosin light chain 2, and myosin light chain 3 in the biological samples, as an indication of the extent of muscle damage in the subject.

Claim 38 (previously presented): The method of claim 35, wherein the evaluating step comprises detecting the presence of at least two different chemical adducts of a myofilament protein in the biological samples.

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Claim 39 (previously presented): The method of claim 38, further comprising the step of assessing a change with time in the amounts of said at least two different chemical adducts of a myofilament protein present in the biological samples, as an indication of the extent of muscle damage in the subject.

Claim 40 (previously presented): The method of claim 38, wherein said at least two different chemical adducts of a myofilament protein are from the same protein.

Claim 41 (previously presented): The method of claim 38, wherein said at least two different chemical adducts of a myofilament protein are from different proteins.

Claims 42-68 (canceled)